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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,087	07/26/2005	Steffen Goletz	10913.0002-00000	7596

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EXAMINER	
SANG, HONG	

ART UNIT	PAPER NUMBER
1643	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/522,087	GOLETZ ET AL.	
	Examiner	Art Unit	
	HONG SANG	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 9-11* is/are pending in the application.

4a) Of the above claim(s) *11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,9 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 July 2005* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

RE: Goletz et al.

1. Applicant's response filed on 4/28/2009 is acknowledged. Claims 1, 2 and 9-11 are pending. Claims 3-8 and 12-13 have been cancelled. Claims 1, 2, and 9-11 have been amended.

2. Newly submitted claim 11 is directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

Claim 11 is drawn to a method of treating tumors comprising administering a composition comprising a MUC1 molecule obtainable by a method according to any one of claims 1 or 2. Applicants elected group I (claims 1-3, 7 and 9-11) in the reply filed on 8/4/2008, which is drawn to a method for the production or identification of a MUC1 molecule which is able to generate an immune response in humans. A method of treating tumors using a MUC1 molecule, and a method of production or identification of a MUC1 molecule using an antibody are distinct because they comprise different steps and use different products. Different method steps and products would require different searches. Moreover, the inventions of these two methods have a separate status in the art because of their different classifications. As such, searching these inventions together would impose serious search burden.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 11 is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

3. Claims 1, 2, 9 and 10 are under examination.

Priority

4. Applicant's submission of an application data sheet which claims priority of European Patent Application No. 02016440.6 is acknowledged.

It is noted that the filing date for PCT/EP03/08014 in the application data sheet appears to be incorrect. The filing date for PCT/EP03/08014 is 7/22/2003, and the publication date for PCT/EP03/08014 is 1/29/2004.

Drawings

5. The objection to the drawings because the "Figure D(2)" on the drawing sheet 11 of 16 should be "Figure 5D(2)" is maintained.

The response states that applicants will correct this figure at a later date.

Objections Withdrawn

6. The objection to the disclosure because the Brief Description of the Drawings does not reference Figures 3A and Figure 3B is withdrawn in view of applicant's amendment to the specification.

7. The objection to claims 7 and 9-11 under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim is withdrawn in view of applicant's amendment to the claims.

8. The objection to claims 9-11 for being dependent from withdrawn claims is withdrawn in view of applicant's amendment to the claims.

Rejections Withdrawn

9. The rejection of claim 11 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, and under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101 is withdrawn in view of applicants amendment to the claim.

10. The rejection of claims 7 and 9-11 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement because the specification does not provide evidence that the claimed antibodies (see claim 7) are (1) known and readily available to the public; (2) reproducible from the written description is withdrawn in view of applicant's amendment to the claims.

11. The rejection of claim 11 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the use of a MUC1 molecule for producing a pharmaceutical composition for the treatment of tumors, does not reasonably provide enablement for the use of a MUC1 molecule for producing a pharmaceutical composition for the prevention of tumors is withdrawn in view of applicant's amendment to the claim.

12. The rejection of claims 1-3 under 35 U.S.C. 102(b) as being anticipated by Snijdewint et al. (Cancer Immunol. Immunother., 1999, 48:47-55), as evidenced by Ryuko et al. (Tumor Biology, 2000, 21, 197-210, IDS) is withdrawn in view of applicant's amendment to the claims.

13. The rejection of claims 1-3, 7 and 9-11 under 35 U.S.C. 103(a) as being unpatentable over Snijdewint et al. (Cancer Immunol. Immunother., 1999, 48:47-55), in view of Ryuko et al. (Tumor Biology, 2000, 21, 197-210, IDS), Chu et al. (US 4,939,240, Date of Patent: 7/3/1990), and Robertson et al. (US 7,402,403B1, Date of Patent: 7/22/2008, earliest effective filing date 5/11/1999) is withdrawn in view of applicant's amendment to the claims.

Objections Maintained

14. The objection to claim 9 because the claims contain non-elected inventions, for example, formulating the cell, the cell lysate or the antibody is maintained because applicants failed to respond to this objection (the objection to claim 10 is withdrawn in view of applicant's amendment to the claim).

New Grounds of Objections and Rejections

Claim Objections

15. Claims 1, 2, 9 and 10 are objected to for reciting "wherein the mixture of MUC1 molecules is a cell line that express and/or secretes tumor associated MUC1 molecule". Contacting a cell line that express and/or secrets tumor associated MUC1 molecule with

an antibody is a step recited in the method for producing cells comprising a MUC1 molecule (see original claim 4, and page 22, last paragraph, for example). The method for producing cells comprising a MUC1 molecule belongs to the inventions of Group II (see Restriction Requirement mailed on 2/4/2008), and thus is not the applicant's elected invention. Furthermore, the specification teach that the term "mixture of MUC1 molecules" comprises a large number of MUC1 molecules which can belong to the same or different species, and such mixtures of MUC1 molecules can preferably be obtained from tissue, tumor cells as well as from cells or cells lines producing inter alia tumor-associated MUC1, and can be cell lysates (see page 6, paragraph 3). The specification does not teach that a mixture of MUC1 molecules can be cell lines. Moreover, one skilled in the art would not refer a mixture of MUC1 molecules to cells.

Appropriate correction is required.

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

17. Claims 1, 2, 9 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Snijdewint et al. (Cancer Immunol. Immunother., 1999, 48:47-55), in view of Ryuko et al. (Tumor Biology, 2000, 21, 197-210, IDS), Torabi-Pour et al. (Biomed. Chromatogr., 2001, 15:18-24), Chu et al. (US 4,939,240, Date of Patent: 7/3/1990), and

Robertson et al. (US 7,402,403B1, Date of Patent: 7/22/2008, earliest effective filing date 5/11/1999).

For this rejection, the term "the mixture of MUC1 molecules" is interpreted as a cell lysate of a cell line that expresses and/or secretes tumor associated MUC1 molecules (see paragraph 15 above).

Snijdewint et al. teach isolation of MUC1 mucin preparation from supernatant of the breast cancer cell line ZR-75-1 cultured for 5 days in serum-free medium, the isolation and purification was done on the basis of molecular size and affinity binding with MUC1 mAb 139H2 (see page 48, column 1, 1st paragraph). Snijdewint et al. disclose that the preparation of MUC1 mucin isolated from the supernatant of the breast cancer cell line ZR-75-1 were tested on PBMC of 3 healthy women and 12 ovarian cancer patients, and no significant effects were seen in the 3 healthy women, in 3 of the ovarian cancer patients a significant stimulating effect was seen (see page 49, column 2, 2nd paragraph, and Figure 3). The MUC1 mAb 139H2 appears to have the recited properties as evidenced by Ryuko et al. (see Figure 2). Snijdewint et al. disclose that MUC1 is a transmembrane glycoprotein expressed on the apical surface of normal glandular epithelial cells, and in the vast majority of human adenocarcinomas, this protein is over-expressed and poorly glycosylated, exposing an immunodominant repetitive amino acid sequence; the overproduction and secretion of MUC1 are correlated to the progression of ovarian, breast and colon carcinoma (see page 47, column 2, paragraph 3).

Snijdewint et al. do not disclose isolation of MUC1 from cell lysate of the breast cancer cell line. Snijdewint et al. do not disclose that the antibody has the recited properties, and further formulating the MUC1 molecule in a pharmaceutically acceptor form or diagnostically applicable form. However, these deficiencies are made up for in the teachings of Ryuko, Torabi-Pour, Chu, and Robertson et al.

Ryuko et al. teach characterization of a new MUC1 monoclonal antibody (VU-2-G7) as well as several known antibodies including A76-A/C7 which are directed to the glycosylated PDTR sequence of MUC1 (see abstract). Ryuko et al. disclose the epitopes to which these antibodies bind, and their reactivity patters with a variety of synthetic nonglycosylated and glycosylated MUC1 peptides (20-mer and 60-mer MUC1 triple tandem repeat peptides, 60-mer 3M GalNAc and 60-mer 9M GalNAc, and modified MUC peptides) (see Table 1 and Figure 2). Ryuko et al. teach that the tested antibodies including A76-A/C7 and 139H2 react with all the MUC1 expressing cancer cell lines (see page 204, column 2, and Figure 4) (which indicates that various cancer cell lines, including breast and ovarian cancer cell lines express surface MUC1). Ryuko et al. teach that the antigen of VU-2-G7, 3M GalNac, may be the choice MUC1 glycopeptide for active immunotherapy (see page 209, last paragraph).

Torabi-Pour et al. teach a method of isolating a tumor antigen from a cell lysate of a tumor cell line expressing said tumor antigen, the method comprises contacting the cell lysate with an antibody that binds specifically to the tumor antigen (see page 19, column 1, last paragraph).

Chu et al. teach isolation and purification of ductal carcinoma antigen from cancer patients using a monoclonal antibody and further formulation of said antigen in an appropriate carrier e.g. saline, with or without human albumin at an appropriate dosage for administration to a patient in a vaccine formulation (see column 14, lines 54-66 and column 30, lines 14-48).

Robertson et al. provide a preparation comprising a human MUC1 protein which MUC1 protein manifests all the antigenic characteristic of a MUC1 protein obtained from the bodily fluids of a patent with advanced breast cancer (see column 7, lines 4-8). Robertson et al. teach that such preparation can be used to detect autoantibodies specific to MUC1 (see column 7, lines 17-31). Robertson et al. teach assay kits suitable for performing the methods fro the detection of autoantibodies, including samples of the tumor marker antigens and means for contacting the sample to be tested with a sample of the antigen (see column 8, lines 13-18). Robertson et al. teach a method of isolation of ABC MUC1 from advanced breast cancer patients comprising purify ABC MuC1 from pooled sera taken from 20 patients with advanced breast cancer using immunoaffinity chromatography with a monoclonal antibody B55 (see Example 1).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Snijdewint et al. to have used the monoclonal antibody A76-A/C7 of Ryuko to isolate MUC1 antigens from a cell lysate of a breast cancer cell line, and further formulated the MUC1 antigens in a pharmaceutically acceptable form or diagnostically applicable form in view of Ryuko, Torabi-Pour, Chu and Robertson et al. One would have been motivated to do so

because Snijdewint and Ryuko teach that MUC1 is a transmembrane glycoprotein overexpressed on breast, and ovarian cancer cells, Ryuko et al. disclose that both A76-A/C7 and 139H2 bind to the same epitope of MUC1 and have similar reactivity patterns with a variety of synthetic non-glycosylated and glycosylated MUC1 peptides, and both antibodies react with all the MUC-1 expressing cancer cell lines. It would have been obvious to simply substitute one known, equivalent antibody for another to obtain predictable results. Moreover, one would have been motivated to formulate the MUC1 antigens in a pharmaceutically acceptable form or diagnostically applicable form for the purpose of treating and diagnosing MUC-1 expressing cancer in view of Chu and Robertson. One of ordinary skill in the art would have a reasonable expectation of success to modify the method of Snijdewint et al. to have used the monoclonal antibody A76-A/C7 of Ryuko to isolate the MUC1 antigens from cell lysate of a breast cancer cell, and further formulated the MUC1 antigens in a pharmaceutically acceptable form or diagnostically applicable form because Snijdewint et al. teach a method of isolation of MUC1 antigens from the supernatant of breast cancer cell line using a monoclonal antibody, Snijdewint and Ryuko teach that MUC1 is a transmembrane glycoprotein overexpressed on breast, and ovarian cancer cells, Torabi-Pour et al. teach how to isolate tumor antigen from cell lysate using an antibody, and the methods of formulation of tumor antigens in a pharmaceutically acceptable form or diagnostically applicable form were well known in the art as shown by the teaching of Chu and Robertson.

Response to Arguments

The response states Snijdewint does not teach that the MUC1 molecule purified from cell culture supernatant are able to generate an immune response in humans.

Applicant's arguments have been carefully considered but are not persuasive. Snijdewint et al. disclose that significant PBMC proliferation can be induced in more than 50% of the ovarian cancer patients by the 20 mer and/or 60mer MUC1 tandem-repeat peptide, which confirms the presence of MUC1-antigen-specific T cells in the blood of ovarian cancer patients. This response is an immune response given the broadest reasonable interpretation of the term "immune response". Furthermore, the MUC1 isolated from breast cancer cell line using the antibody taught by Ryuko such as A76-A/C7 appears to be the same as that produced by the instant methods (which is isolated from tumor cell line using the A76-A/C7), as such it would inherently have the same property.

The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the MUC1 isolated from cell lysate of breast cancer cell line using antibodies of Ryuko such as A76-A/C7 are not the same as the isolated by the claimed methods. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed markers are different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Conclusion

18. No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to HONG SANG whose telephone number is (571)272-8145. The examiner can normally be reached on 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Hong Sang/
Examiner, Art Unit 1643

/Christopher H Yaen/
Primary Examiner, Art Unit 1643